UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

ELI LILLY AND COMPANY, Plaintiff, vs. TEVA PARENTERAL MEDICINES, INC., APP PHARMACEUTICALS, LLC, PLIVA HRVATSKA D.O.O., TEVA PHARMACEUTICALS USA INC., BARR LABORATORIES, INC., Defendants.	)	No. 1:10-cv-01376-TWP-DKL

ENTRY ON MOTIONS *IN LIMINE*

This matter is before the Court on two Motions *in Limine* (Dkts. 235 & 244) filed by Defendants App Pharmaceuticals, LLC, Barr Laboratories, Inc., Pliva Hrvatska D.O.O., Teva Parenteral Medicines, Inc., and Teva Pharmaceuticals USA Inc. The Court will address each motion in turn, and will address additional facts relevant to each motion as needed.

I. BACKGROUND

This is a patent infringement case involving the administration of pemetrexed disodium ("pemetrexed"), which Plaintiff Eli Lilly and Company ("Lilly") markets as the drug ALIMTA® for the treatment of malignant pleural mesothelioma. U.S. Patent No. 7,772,209 (the "'209 patent" or "patent-in-suit") covers the administration of folic acid and vitamin B_{12} followed by the administration of pemetrexed, which reduces the toxicity of pemetrexed. Lilly obtained the '209 patent-in-suit in August 2010. Lilly sued Defendants for infringement of the '209 patent after Defendants' filed Abbreviated New Drug Applications ("ANDAs") seeking United States

Food & Drug Administration ("FDA") approval to sell generic versions of Lilly's ALIMTA® treatment before the expiration of the '209 patent.

Defendants contend that the asserted claims of '209 patent are obvious under 35 U.S.C. § 103, and thus are invalid, based on prior art references that teach the use of pemetrexed with folic acid, in combination with references that suggest combining that regimen with vitamin B_{12}. In response, Lilly has indicated its intent to introduce evidence of purported objective indicia of non-obviousness, otherwise known as secondary considerations, including unexpected results and commercial success. At trial, Lilly intends to argue that these secondary considerations weigh against finding that the asserted claims of the '209 patent are invalid for obviousness. The trial in this matter, scheduled to begin on August 19, 2013, is a bench trial as opposed to a trial by jury.

II. LEGAL STANDARD

The Court excludes evidence on a motion *in limine* only if the evidence clearly is not admissible for any purpose. *See Hawthorne Partners v. AT&T Techs., Inc.*, 831 F. Supp. 1398, 1400 (N.D. Ill. 1993). Unless evidence meets this exacting standard, evidentiary rulings must be deferred until trial so questions of foundation, relevancy, and prejudice may be resolved in context. *Id*. at 1400–01. Moreover, denial of a motion *in limine* does not necessarily mean that all evidence contemplated by the motion is admissible; rather, it only means that, at the pretrial stage, the court is unable to determine whether the evidence should be excluded. *Id*. at 1401.

In addition, where, as here, the proceeding is a bench trial, the court has leeway to provisionally admit testimony or evidence and to disregard later if, upon reflection, it should have been excluded. *Mintel Intern. Group, Ltd. V. Neergheen,* 636 F.Supp2d 677 (N.D.Ill.2009).

Where the gatekeeper and the factfinder are one and the same—that is, the judge—the need to make such decisions prior to hearing the testimony is lessened. See *United States v. Brown*, 415 F.3d 1257, 1268–69 (11th Cir.2005). With these guidelines in mind, the Court turns to the motions before it.

III. DISCUSSION

A. Defendants' First Motion *in Limine* (Dkt. 235)

Defendants request the Court preclude Lilly from proffering testimonial evidence of its experts, Dr. Steven H. Zeisel and Dr. Peter J. O'Dwyer, regarding alleged unexpected results as evidence of the non-obviousness of the '209 patent, arguing that their proposed testimony is irrelevant as a matter of law because their analyses are not based upon the closest prior art. Before Lilly applied for the '209 patent, Lilly, its affiliates, and other researchers published results of a clinical study describing the administration of pemetrexed with folic acid pretreatment to cancer patients (the "Hammond abstracts"). In this study, patients received 90 courses of 5 milligrams per day of folic acid for five days starting two days before pemetrexed therapy. The Defendants assert that the Hammond abstracts are "prior art" for the '209 patent, and that the claims of the '209 patent are obvious under 35 U.S.C. § 103 based upon the teachings in the Hammond abstracts. For example, Defendants contend that there would have been a motivation to add the vitamin B_{12} pretreatment to the pemetrexed and folic acid pretreatment regimen disclosed in the Hammond abstracts. Lilly proposes to present evidence that the addition of B_{12} and reduction of the folic acid dosage produced unexpected results; thus the '209 patent is not obvious and therefore not invalid.

In order to show unexpected results, the law requires a comparison with the closest prior art. *Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 970 (Fed. Cir. 2006). If the prior art would not

have taught or suggested the claimed invention to a person of ordinary skill in the relevant art, the challenger's obviousness case necessarily fails. *See Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012). Based upon the reports of Lilly's experts, Defendants anticipate that Lilly will present testimony purportedly comparing the properties or expected properties of the methods of use claimed in the '209 patent to the properties of pemetrexed alone, as opposed to comparing it to the methods in the Hammond abstracts using the folic acid pretreatment with pemetrexed. In particular, Defendants assert that Lilly's experts will likely testify that the addition of folic acid and vitamin B_{12} supplementation to the use of pemetrexed alone unexpectedly reduced pemetrexed's toxicity without compromising its efficacy. Defendants argue Lilly's evidence of these unexpected results is not based on a comparison with the closest prior art, which they assert are the Hammond abstracts, and should thus be excluded as irrelevant.

Defendants are essentially asking the Court to determine, as a matter of law, the closest prior art to the '209 patent. In order to determine what constitutes "closest prior art" the Court must determine how the putative closest references are "viewed as they would be perceived by persons experienced in the particular field of science." *Astrazeneca Pharm. LP v. Teva Pharm. USA, Inc.*, 583 F.3d 766, 775 (Fed. Cir. 2009). The Court cannot make this factual determination by simply comparing the elements of each process and applying a lay person's opinion based on a one-to-one comparison. "[A] district court must *always* consider any objective evidence of nonobviousness presented in a case." *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Contractors USA, Inc.*, 617 F.3d 1296, 1305 (Fed. Cir. 2010) (emphasis in original). The Court finds that the opinions of Dr. O'Dwyer and Dr. Zeisel are relevant to the issues of which prior art a person of ordinary skill in the art would consider to be closest to the '209 patent, and what a

person of ordinary skill would have expected the results of the '209 patent process to be based upon what was known in June 1999. These factual questions go to the ultimate issue of whether the results obtained with the claimed invention would have been unexpected, thus rebutting the Defendants' claim of obviousness.

In addition, Defendants ask the Court to exclude the testimony of Dr. Zeisel on unexpected results because he did not consider the data regarding the claimed methods after June 1999, and therefore his testimony is conclusory and lacks a factual basis. Lilly argues that Defendants have misconstrued the purpose of Dr. Zeisel's opinion. Lilly asserts that Dr. Zeisel was not asked to perform an analysis comparing different pemetrexed regimens; rather, the purpose of his testimony is to show what a person of ordinary skill—specifically, a nutritionist—would expect regarding the addition of the folic acid and/or vitamin B_{12} pretreatment to an antifolate cancer chemotherapy regimen based on the known art in June 1999. Lilly also asserts that Dr. Zeisel's testimony is being offered to show that a person of ordinary skill would not have reason to make the invention covered by the '209 patent. Defendants have not shown that Dr. Zeisel's testimony would not be relevant for any purpose, and as stated above, this testimony is relevant to the issue of obviousness and should therefore not be excluded prior to trial.

B. Defendants' Second Motion *in Limine* (Dkt. 244)

In their second Motion *in Limine,* Defendants ask the Court to preclude Lilly from proffering evidence of alleged commercial success of the '209 patent because it is not relevant in this case. Commercial success is another secondary consideration in determining whether a patent is invalid for obviousness. Generally, commercial success is relevant because the law presumes an idea would have been brought to market sooner had the idea been obvious to persons skilled in the art; thus evidence of commercial success and some causal relationship between the invention

and commercial success of a product embodying that invention is probative of whether an invention was non-obvious. *Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1376 (Fed. Cir. 2005).

Defendants argue that Lilly has not established a nexus between ALITMA®'s commercial success and the vitamin pre-treatment regimen claimed in the '209 patent. To demonstrate a nexus between commercial sales and the patent-in-issue, Lilly must provide evidence that it is the novel aspect of the patent, and not attributes that were already present in the prior art, that drive the commercial sales. *See Tokai Corp. v. Easton Enters., Inc.*, 632 F.3d 1358, 1369 (Fed. Cir. 2011) ("If commercial success is due to an element in the prior art, no nexus exists."). "[A] presumption arises that the patented invention is commercially successful '[w]hen a patentee can demonstrate commercial success, usually shown by significant sales in a relevant market, and that the successful product is the invention disclosed and claimed in the patent.'" *Ecolochem, Inc. v. S. Cal. Edison Co.*, 227 F.3d 1361, 1377 (Fed. Cir. 2000) (quoting *J.T. Eaton & Co. v. Atlantic Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997)). The burden is on the defendant, not the plaintiff, to show that the commercial success claimed by the Plaintiff is due solely to factors not claimed in the patented invention. *Id.* Lilly states that its expert, Dr. Grabowski, will testify not that the commercial success is attributable solely to the addition of B_{12} to the pretreatment regimen; but rather that the novel aspects of the '209 patent have allowed a greater number of patents to receive treatment using pemetrexed, demonstrating commercial success. Therefore, Lilly's expert's testimony that ALIMTA® had commercial success is relevant and should not be excluded.

Finally, Defendants argue that evidence of this secondary consideration is irrelevant in this case because the presumption associated with commercial success does not apply if other patents

"blocked" a person of ordinary skill in the art from practicing the claimed "invention." Financial success is not significantly probative where others were legally barred from commercially testing the claimed invention. *Merck & Co.*, 395 F.3d at 1377. There are two earlier Lilly patents relevant to pemetrexed, U.S. Patent No. 5,344,932 (the "'932 patent") for the compound pemetrexed disodium, and U.S. Patent No. 5,217,974 (the "'974 patent") claiming, *inter alia*, a method of using pemetrexed disodium with folic acid to inhibit growth of certain tumors and reducing the toxicity of ALIMTA®. Defendants argue that the '932 patent and the '974 patent made it impossible for any other person or entity to commercially test or market a method of using pemetrexed with folic acid for any purpose, including the use of pemetrexed disodium claimed in the '209 patent, thus rendering the factor of commercial success irrelevant in this case.

Lilly asserts that Dr. Grabowski will testify that there was some financial incentive for others to make the claimed invention, and while the '932 patent would have prevented competitors from marketing pemetrexed, a third party would not have been prevented from developing and patenting the vitamin supplementation regimen in the '209 patent and then licensing it to Lilly, and would have been able to test the regimen under the safe harbor provision of the Hatch-Waxman Act, 35 U.S.C. § 271(e)(1). Defendants cite *Merck* in support of their argument that this evidence is irrelevant and inadmissible due to Lilly's blocking patents; however, in *Merck*, the Federal Circuit found that the district court had misjudged the weight of the commercial success factor in its conclusion of non-obviousness under the specific facts of the case, not that the evidence was entirely inadmissible. *Merck & Co.*, 395 F.3d at 1377. Likewise, in this case, the presence of the blocking patents goes to the weight to be afforded to Lilly's

evidence of commercial success, not its admissibility. Therefore, Dr. Grabowski's testimony is relevant and should not be excluded.

IV. CONCLUSION

For the foregoing reasons, Defendants' Motions *in Limine* (Dkts. 235 & 244) are **DENIED**.

SO ORDERED.

Date: 07/29/2013

Hon. Tanya Walton Pratt, Judge
United States District Court
Southern District of Indiana

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